

HM

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FIGURE 1

mAb	Mean Fluorescence Intensity			% Gated
	L1.2-CCR5	PBMC	L1.2-CCR5	
mouse IgG1	10	4	1	1
2D7	75	29	92	36
PA8	48	9	73	3
PA9	79	5	96	3
PA10	80	8	96	5
PA11	107	8	96	10
PA12	115	8	96	8
PA14	81	14	96	22

FIGURE 2

2019B233615 - 0631601

INHIBITOR COMBINATION	CONCENTRATION RATIO	ASSAY	COMBINATION INDEX	
			90% Inhibition	50% Inhibition
PA12:2D7	10:1	Entry	0.043	0.291
	2:1	Fusion	0.017	0.019
	10:1	Fusion	0.087	0.067
	50:1	Fusion	0.158	0.046
PA12:PA14	10:1	Entry	0.437	0.535
	10:1	Fusion	0.22	0.263
PA14:2D7	1:1	Entry	2.85	1.85
	1:1	Fusion	1.34	1.74
PA12:PA11	1:1	Entry	0.707	0.641
PA12:RANTES	1000:1	Fusion	0.331	0.156
	100:1	Fusion	1.6	1.37
	100:1	Fusion	0.972	0.962
PA12:CD4-IgG2	10:1	Fusion	0.3	0.31
PA14:CD4-IgG2	1:1	Fusion	0.957	0.566
2D7:CD4-IgG2	1:1	Fusion	1.127	0.302

FIGURE 3

Epitopes	IC ₅₀ values (μg/ml)			
	cell-cell fusion inhibition	viral entry inhibition	gp120-binding inhibition	calcium flux inhibition
PA8 Nt	-	-	-	-
PA9 Nt/ECL2	-	-	0.24	-
PA10 Nt/ECL2	-	-	0.13	-
PA11 Nt	25.5	-	0.33	-
PA12 Nt	10.0	-	0.24	-
PA14 Nt/ECL2	1.7	.024	1.58	6.4
2D7 ECL2	1.6	.026	1.38	45

FIGURE 4

		1	5	10	15	20	25	30																								
		M	D	Y	Q	V	S	S	P	I	Y	D	I	N	Y	Y	T	S	E	P	C	Q	K	I	N	K	Q	I	A	A	A	R
Nt		2D7	92	54	90	nd	83	63	82	nd	46	40	nd	40	90	90	86	111	49	57	45	44	37	52	27	92	nd	nd	nd	65		
ECL1		PA8	118	63	78	nd	52	36	32	nd	4	2	nd	0	53	2	45	100	47	32	36	44	57	54	24	13	nd	nd	nd	36		
ECL2		PA9	16	13	0	nd	213	19	13	nd	10	0	nd	19	62	52	29	73	36	32	36	45	30	55	18	145	nd	nd	nd	40		
ECL3		PA10	21	4	0	nd	175	59	22	nd	14	8	nd	15	101	48	49	94	27	47	45	45	39	53	13	133	nd	nd	nd	46		
ECL3		PA11	70	32	0	nd	112	80	81	nd	40	22	nd	51	74	70	46	85	32	47	36	48	40	47	22	146	nd	nd	nd	44		
ECL3		PA12	68	30	0	nd	76	81	51	nd	34	12	nd	49	76	68	40	86	30	41	49	46	34	54	12	93	nd	nd	nd	43		
ECL3		PA14	9	86	75	nd	85	88	89	nd	37	40	nd	64	78	84	66	76	80	71	44	86	64	76	46	99	nd	nd	nd	33		
			90	95	100																											
		H	Y	A	A	A	Q	W	D	F	G	N	T	M	C	Q																
ECL1		2D7	70	89	nd	nd	nd	nd	40	130	40	66	nd	58	72	82	0	74														
ECL2		PA8	38	92	nd	nd	nd	nd	45	118	32	115	nd	96	86	68	10	39														
ECL3		PA9	31	66	nd	nd	nd	nd	27	81	15	199	nd	130	89	57	0	43														
ECL3		PA10	37	83	nd	nd	nd	nd	36	139	18	133	nd	112	97	61	0	40														
ECL3		PA11	39	81	nd	nd	nd	nd	38	91	25	78	nd	60	94	71	10	60														
ECL3		PA12	63	67	nd	nd	nd	nd	35	91	29	77	nd	76	79	102	25	55														
ECL3		PA14	73	79	nd	nd	nd	nd	63	83	23	86	nd	47	89	80	9	77														
			170	175	180	185	190																									
		R	S	Q	K	E	G	L	H	Y	T	C	S	S	H	F	P	Y	S	Q	Y	Q	F	W	K	N	F	Q				
ECL2		2D7	62	55	17	0	nd	nd	62	64	65	0	83	95	53	32	32	80	92	73	92	34	73	39	33	45	102					
ECL3		PA8	38	40	58	31	nd	nd	65	63	63	26	90	100	51	51	46	90	69	74	59	38	95	33	40	27	62					
ECL3		PA9	39	28	63	15	nd	nd	34	13	0	29	93	112	77	53	77	79	61	73	74	73	31	38	12	35	38					
ECL3		PA10	45	59	34	19	nd	nd	30	21	0	25	84	96	32	61	39	77	82	53	68	16	39	45	16	50	70					
ECL3		PA11	67	58	55	33	nd	nd	49	138	130	37	78	95	50	48	38	91	99	61	34	24	73	47	23	50	92					
ECL3		PA12	52	56	36	31	nd	nd	32	102	126	39	73	85	44	49	42	101	90	45	56	23	66	37	28	33	74					
ECL3		PA14	17	85	88	59	nd	nd	80	24	72	9	109	83	52	64	50	90	93	88	65	34	79	55	51	72	71					
			265	270	275																											
		Q	E	F	F	G	L	N	N	C	S	S	S	N	R	L	D	Q														
ECL3		2D7	63	35	29	nd	nd	nd	77	61	60	71	71	78	68	77	nd	156														
ECL3		PA8	78	25	9	nd	nd	nd	37	53	42	85	71	73	86	99	nd	98														
ECL3		PA9	52	22	1	nd	nd	nd	67	40	50	71	81	77	90	93	nd	112														
ECL3		PA10	41	25	4	nd	nd	nd	64	60	56	93	10	49	74	72	nd	128														
ECL3		PA11	60	28	0	nd	nd	nd	35	60	49	78	72	70	72	75	nd	166														
ECL3		PA12	60	28	1	nd	nd	nd	34	36	46	83	72	99	82	78	nd	131														
ECL3		PA14	92	82	42	nd	nd	nd	80	31	92	106	90	98	74	78	nd	112														

76%-100+%

51%-75%

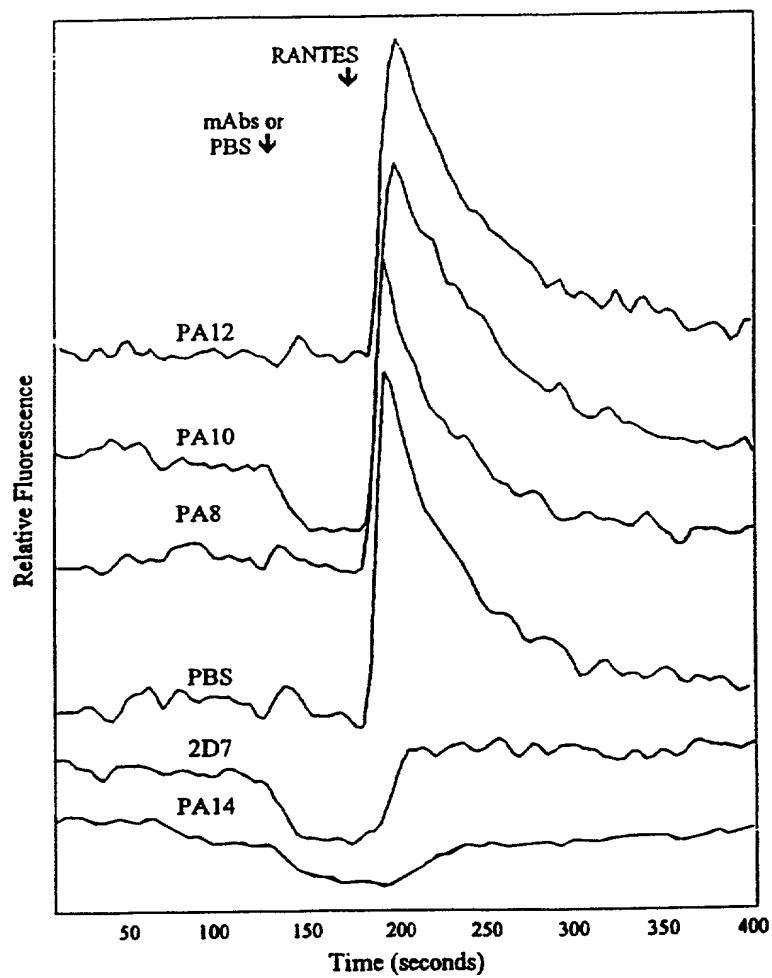
26%-50%

0%-25%

nd

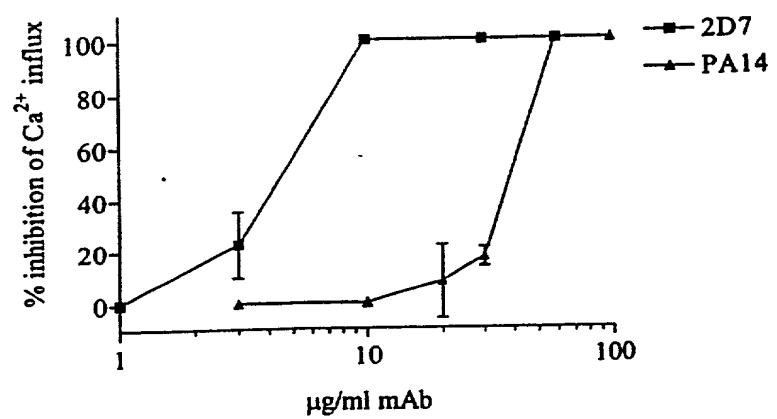


FIGURE 5A



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FIGURE 5B



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FIGURE 6A

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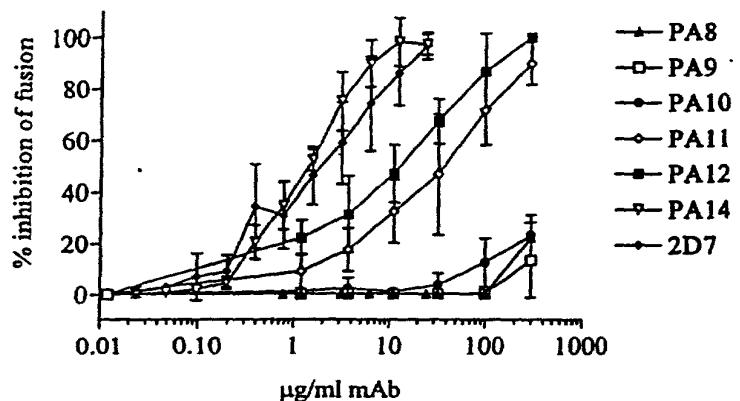
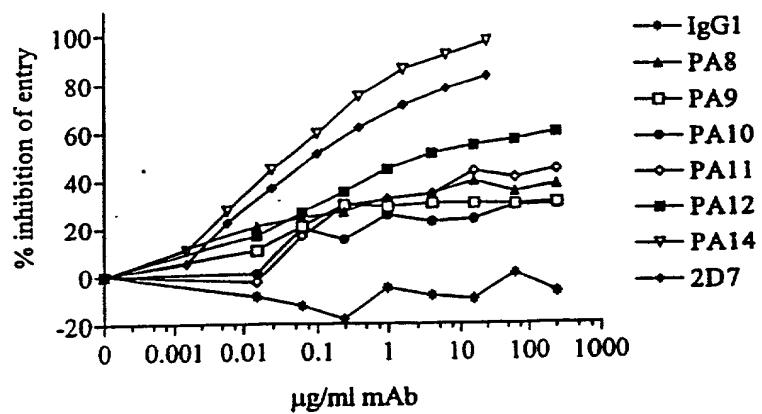
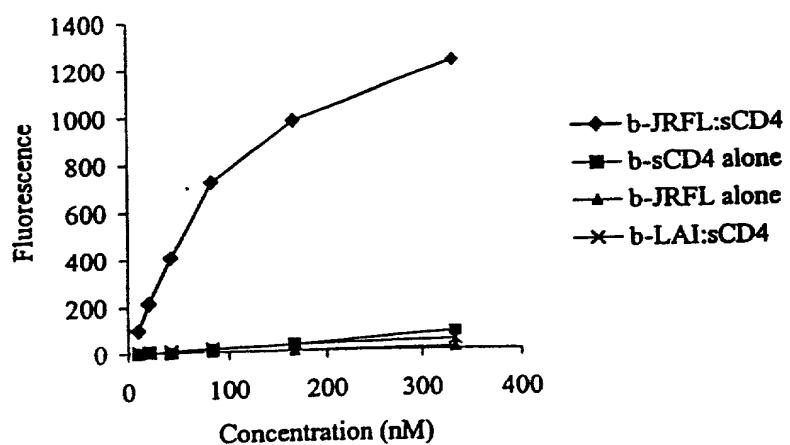


FIGURE 6B

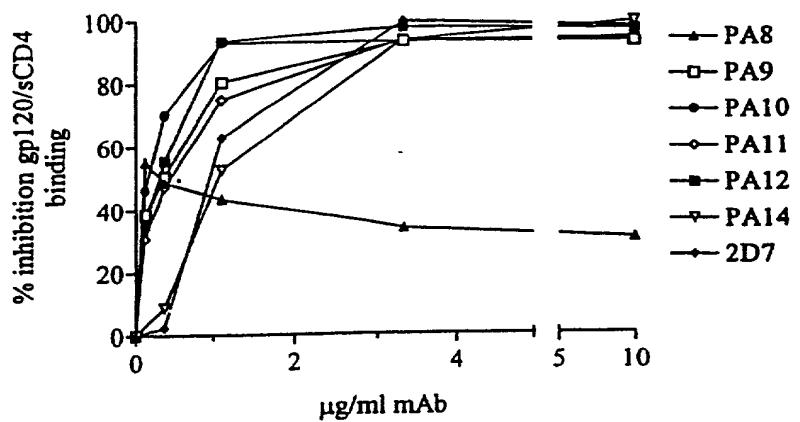
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FIGURE 6C



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FIGURE 6D



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FIGURE 7

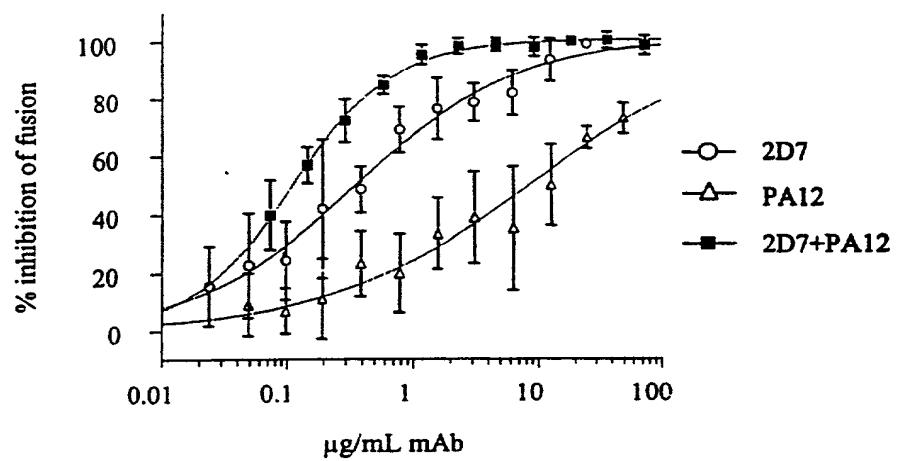


FIGURE 8

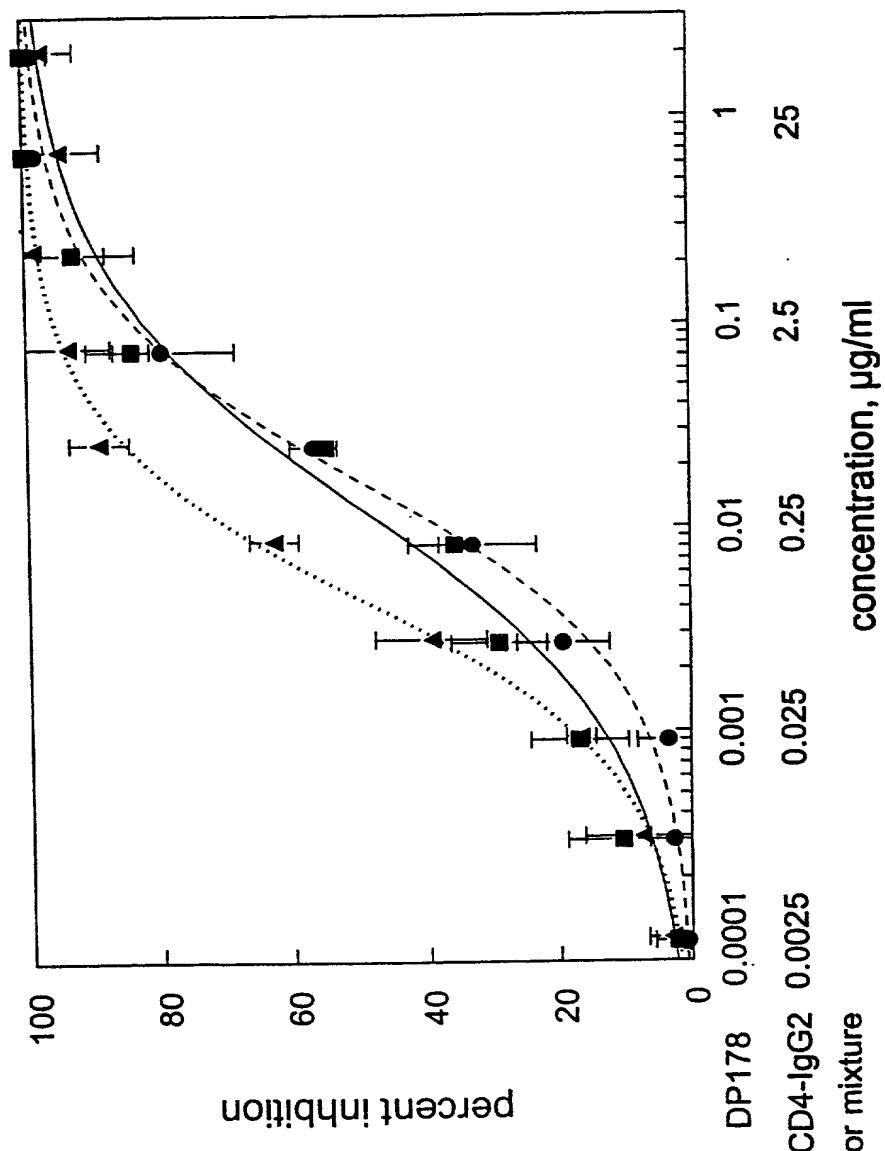


FIGURE 9

Percent Inhibition	Combination Index			
	CD4-IgG2:T-20 Mass Ratio			
	25:1 (low)	25:1 (high)	5:1	1:1
95	0.32	0.20	0.22	0.50
90	0.38	0.25	0.27	0.55
85	0.43	0.29	0.30	0.59
80	0.47	0.33	0.34	0.62
75	0.51	0.36	0.37	0.65
70	0.54	0.39	0.40	0.67
65	0.58	0.42	0.43	0.70
60	0.61	0.45	0.45	0.73
55	0.65	0.48	0.49	0.75
50	0.69	0.51	0.52	0.78

FIGURE 10

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Percent Inhibition	T-20			CD4-IgG2		
	Concentration, $\mu\text{g/ml}$	Dose Reduction	Concentration, $\mu\text{g/ml}$	Dose Reduction	Concentration, $\mu\text{g/ml}$	Dose Reduction
99	1.1	0.17	6.6	130	4.3	29
95	0.21	0.044	4.9	19	1.10	17
90	0.10	0.024	4.2	7.8	0.59	13
70	0.025	0.0076	3.3	1.6	0.19	8.4
50	0.011	0.0039	2.8	0.60	0.095	6.3

FIGURE 11A

Percent Inhibition	Combination Index	PRO 542			PA12			T-20		
		Concentration, nM		Dose Reduction	Concentration, nM		Dose Reduction	Concentration, nM		Dose Reduction
		Alone	Mix		Alone	Mix		Alone	Mix	
95	0.41	10	2.1	4.8	730	2.8	260	94	19	4.9
90	0.45	7.0	1.6	4.4	320	2.1	150	63	14	4.5
70	0.47	4.1	0.92	4.5	72	1.2	60	30	8.1	3.7
50	0.48	3.1	0.66	4.7	28	0.87	32	19	5.8	3.3

PRO 542, PA12 and T-20 were used in an approximate 1:1:10 molar concentration ratio.

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FIGURE 11B

Percent Inhibition	Combination Index	PRO 542				PRO 140				T-20			
		Concentration, nM		Concentration, nM		Dose Reduction		Dose Reduction		Concentration, nM		Dose Reduction	
		Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix	Alone	Mix
95	0.40	8.5	1.9	4.5	19	1.0	19	140	17	8.2			
90	0.39	7.1	1.5	4.7	13	0.77	17	100	13	7.7			
70	0.37	5.3	0.87	6.1	7.2	0.46	16	57	7.7	7.4			
50	0.35	4.6	0.63	7.3	4.9	0.34	14	40	5.6	7.1			

PRO 542, PRO 140 and T-20 were used in an approximate 2:1:20 molar concentration ratio.

FIGURE 11C

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Percent Inhibition	Combination Index	PRO 542			PRO 140			T-20		
		Concentration, nM		Dose Reduction	Concentration, nM		Dose Reduction	Concentration, nM		Dose Reduction
		Alone	Mix		Alone	Mix		Alone	Mix	
95	0.24	61	2.5	24	11.9	0.72	17	156	22	7.1
90	0.22	32	1.4	23	8.4	0.40	21	96	13	7.4
70	0.19	9.8	0.50	20	4.5	0.14	32	40	4.5	8.9
50	0.18	4.7	0.26	18	3.0	0.074	41	23	2.3	10

PRO 542, PRO 140 and T-20 were used in an approximate 4:1:30 molar concentration ratio.

FIGURE 11D

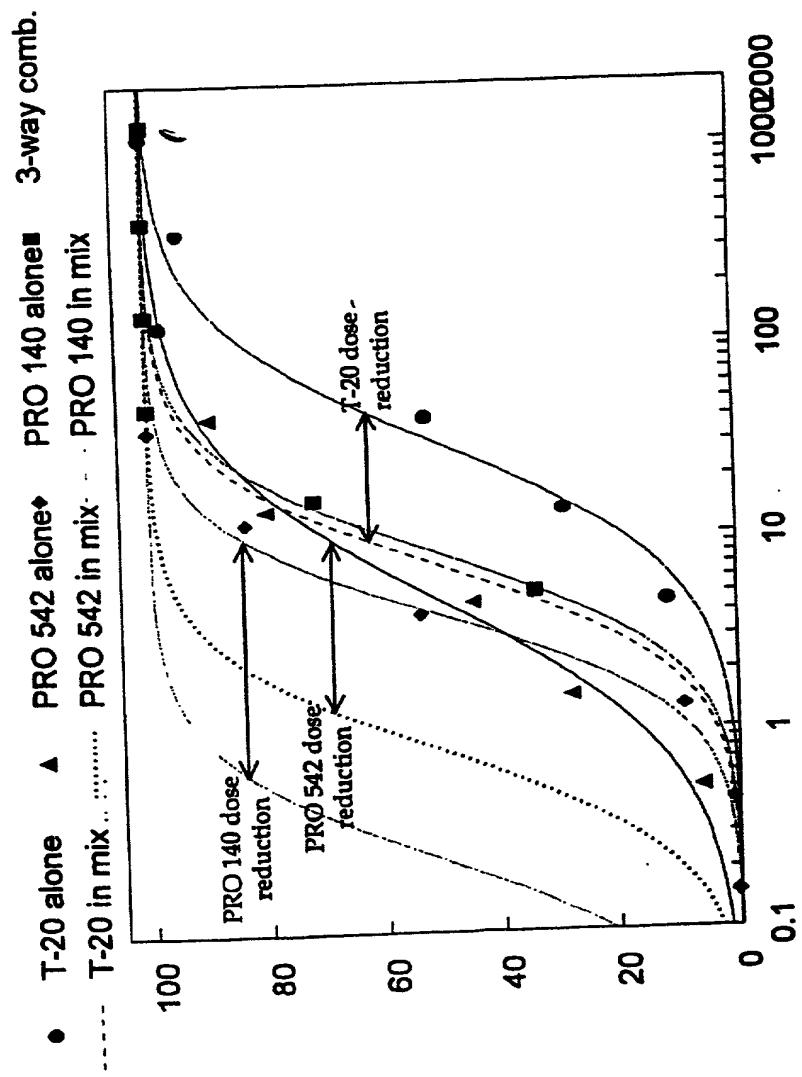
Percent Inhibition	Combination Index	PRO 140			T-20		
		Concentration, nM		Dose Reduction	Concentration, nM		Dose Reduction
		Alone	Mix		Alone	Mix	
95	0.56	12	1.8	6.7	156	55	2.8
90	0.55	8.4	1.1	7.4	96	35	2.7
70	0.55	4.5	0.51	8.8	40	16	2.5
50	0.56	3.0	0.31	9.9	23	10	2.4

PRO 140 and T-20 were used in an approximate 1:30 molar concentration ratio.

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FIGURE 12

Triple Combination Synergistically Blocks HIV-1 Entry (I)



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FIGURE 13

